Peculiar Histological Features of Oral Intravascular Papillary Endothelial Hyperplasia

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ABSTRACT: A 55-year-old male patient with single and well-circumscribed nodule in the lower lip. Accurate diagnosis is based only on histopathological examination using hematoxylin and eosin and immunohistochemical approach, which a large, organized thrombus within the dilated lumen of a poorly demarcated vein, associated with papillary projections of endothelial proliferation occupying vascular spaces. The final diagnosis was intravascular papillary endothelial hyperplasia (IPEH) associated with a thrombus. Oral IPEH is rare and has historically been difficult to diagnose due to its resemblance to other oral lesions. However, the distinctive histological features of oral IPEH associated with a thrombus now allow for its diagnosis through hematoxylin and eosin staining alone, without the need for additional techniques. Therefore, it is crucial for pathologists to be familiar with these unique morphological features to accurately diagnose oral IPEH and differentiate it from more common benign, malignant, or reactive vascular lesions in the oral cavity.

KEYWORDS: Oral intravascular papillary endothelial hyperplasia, Masson's tumor, oral lesion, differential diagnosis

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Intravascular papillary endothelial hyperplasia (IPEH) is a unique form of thrombus organization characterized by the proliferation of endothelial cells in a papillary pattern within the vascular lumen.[1] The pathogenesis of IPEH and the reason for its development only in certain thrombi has not been completely established.[2,3] Particularly in the oral cavity, the presence of thrombus associated with veins is considered a rare occurrence, and there are fewer than 130 cases of IPEH reported in the literature.[1] The definitive diagnosis of IPEH can be achieved through conventional histopathological analysis using hematoxylin and eosin (H&E) staining, sometimes supplemented by immunohistochemistry techniques.[3] We describe a case of oral IPEH, highlighting its peculiar morphological features observed in different histological staining, with the aim of assisting all surgical pathologists in its accurate diagnosis, particularly in routine H&E staining.

A 55-year-old male patient was referred to the dentist for evaluation of a single and well-circumscribed nodule normochromic in the lower lip. The nodule was painless, covered by normal oral mucosa, had been present for 1 year, and clinically diagnosed as a mucocele. An excisional biopsy was performed, and the surgical specimen was submitted for histopathological analysis. The histopathological examination of the sections stained with H&E showed a large, organized thrombus within the dilated lumen of a poorly demarcated vein, associated with papillary projections of endothelial proliferation occupying vascular spaces (Figures 1A and 1C). There was no evidence of cellular atypia or abnormal mitosis in the endothelial cells. Masson's trichrome staining was performed and confirmed the H&E findings, highlighting mainly the mature collagen fibers distributed both in the bluish round thrombus and among proliferating endothelial cells (Figures 1B and 1D). The smooth muscle cells of the vein wall and the fibrin within the thrombus were stained red on Masson's trichrome. Additionally, the immunohistochemical marker CD31 was used to identify the prominent vascular channels lined by a simple layer of endothelium (Figure 1E), and alpha-smooth muscle actin positivity confirmed the papillary vascular formation (Figure 1F). The final diagnosis was intravascular papillary endothelial hyperplasia associated with a thrombus in the lower lip. Clinical follow-up for 1 year showed no recurrence.

Although oral IPEH has been considered rare[1], it is probably underreported. Over the years, the pathogenesis of oral IPEH has been strongly linked to local trauma/microtrauma, which induces injury to the vessel wall,2 however, in our patient the history of local trauma was not confirmed. Based on histological features, IPEH has been classified into 3 subtypes: pure IPEH, characterized by dilated vascular veins with associated thrombus; mixed IPEH, displaying focal changes in preexisting vascular lesions like pyogenic granuloma; and extravascular IPEH, a rare condition occurring during hematoma organization.[1] In our case report, there is no histological doubt that it is a pure IPEH associated with a thrombus in the lower lip. However, most studies in the literature do not differentiate the types of oral IPEH or provide microscopic evidence of the thrombus.[3] In our patient, Masson's trichrome staining contributed to identifying the proliferation of smooth muscle cells and the deposition of collagen in the IPEH associated with the organized

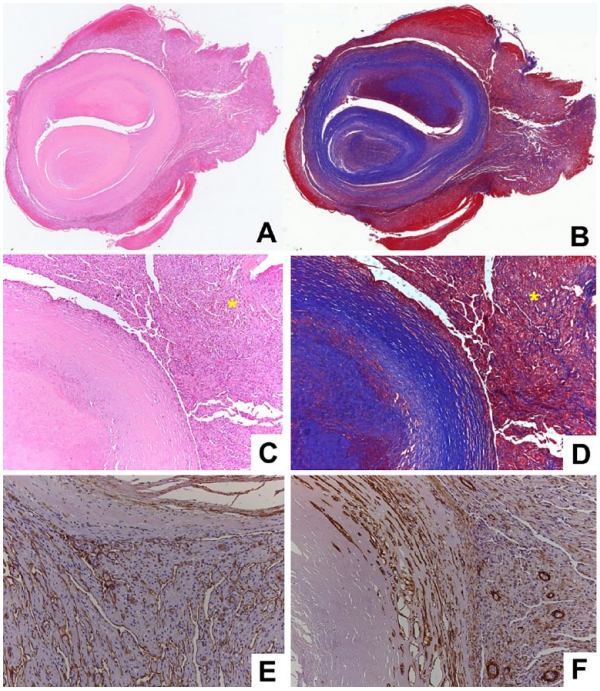

Figure 1. Histological features of pure intravascular papillary endothelial hyperplasia: (A and B) the photomicrographic sections showed thrombus in organization with well-defined papillary proliferations of endothelial cells within in the lumen of the dilated vein, (C and D) illustrate peculiar features, in higher magnification, of the papillary vascular structures (yellow asterisk) associated with the thrombus. In D, the Masson's trichrome identified the collagen fibers both in the bluish round thrombus and in endothelial papillary hyperplasia. Details of the vascular channels lined by endothelium can be observed by immunopositivity of CD31 (E) and alpha-smooth muscle actin (F) markers. (Original magnification, Hematoxylin and Eosin: A = 2.5× and C = 10×; Masson's trichrome: B = 2.5× and D = 10×; Immunohistochemistry: E = CD31—20× and F = alpha-smooth muscle actin—10×)

thrombus. Additionally, the utilization of immunohistochemical markers confirmed the vascular origin of the papillary proliferation associated with the thrombus. Although the use of immunohistochemical markers is not crucial for the diagnosis of oral IPEH, they are often used to rule out malignancy.[1]

Oral IPEH is uncommon, but its distinct histological features, particularly in association with a thrombus, allow for diagnosis using H&E without additional histological staining techniques. Pathologists must be familiar with these microscopic features to accurately distinguish IPEH from other benign, malignant, or reactive oral vascular lesions.

Author Contributions

G.L.S. and K.A.P. wrote the manuscript with inputs from all authors; D.T.O. revised it critically for important intellectual content, performed the histopathological analysis, and contributed to the lesion diagnosis; C.T.S. performed the immunohistochemistry analysis. Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content.

Consent to Participate

Informed consent was obtained from the patient.

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